REMARKS

Introductory Comments:

Claims 1-15 and 41 were examined in the Office Action under reply and rejected under (1) 35 U.S.C. §112, second paragraph (claims 1-15 and 41); and (2) 35 U.S.C. §102 (claims 1-13 and 41). These rejections are believed to be overcome by the above amendments and are otherwise traversed for reasons discussed below.

Overview of the Above Amendments:

Claims 1, 3, 14 and 15 have been amended in order to recite the invention with greater particularity. Claims 8 and 9 have been canceled and the substance thereof incorporated into claims 1 and 3. Claims 14 and 15 have been amended to depend from claims 1 and 3, respectively, for antecedent basis purposes. The above amendments are made without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record.

The specification has been amended to insert sequence identification numbers.

Formal Matters:

The Office requested a Sequence Listing in compliance with 37 CFR §1.821-1.825. A Sequence Listing accompanies this response.

Rejections Under 35 U.S.C. §112, Second Paragraph:

Claims 1-15 and 41 were rejected under 35 U.S.C. §112, second paragraph "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Office Action, page 3. In particular, the Office argues that the term "sustained" is not clearly defined in the specification. Applicant disagrees. The Office's attention is directed to page 7, first full paragraph, where "sustained expression or presence" is defined as at least about one month in duration. Thus, the term is sufficiently clear and applicant respectfully requests withdrawal of this basis for rejection.

Claims 14 and 15 were rejected under 35 U.S.C. §112, second paragraph as indefinite for lacking antecedent basis. These claims have been amended to depend from claims 1 and 3, respectively, as suggested by the Office. Thus, this basis for rejection has been overcome and withdrawal thereof is requested.

Rejections Over the Art:

Claims 1-13 and 41 were rejected under 35 U.S.C. §102(b) as anticipated by Lee et al., *Hepatology* (June 2000) 31:1327-1333 ("Lee"). Applicant notes that this article published less than one year prior to applicant's priority date of June 27, 2000. Accordingly, the rejection under 35 U.S.C. §102(b) is in error. Moreover, the inventor of the present application, Paliard, is a coauthor on Lee and the relevant portions of Lee describe applicant's own work. To evidence this, applicant is submitting the Declaration of Xavier Paliard, pursuant to *In re Katz*. Thus, this basis for rejection has been overcome. Withdrawal of the rejection over Lee is respectfully requested.

Claims 1, 3, 6, 7, 12, 13 and 41 were rejected under 35 U.S.C. §102(b) as anticipated by Feitelson et al., *J. Virol.* (1988) 62:1408-1415 ("Feitelson"). Additionally, claims 1, 3-5 and 41 were rejected under 35 U.S.C. §102(b) as anticipated by Yanagi et al., *Proc. Natl. Acad. Sci.* (1997) 94:8738-8743 ("Yanagi"). Applicant notes that claims 8 and 9 are not subject to the rejections over Feitelson and Yanagi. The substance of these claims has been incorporated into independent claims 1 and 3. All remaining claims ultimately depend from claims 1 or 3. Thus, these bases for rejection have been overcome and withdrawal thereof is respectfully requested.

CONCLUSION

Applicant respectfully submits that the claims are novel and nonobvious over the art and comply with the requirements of 35 U.S.C. §112. Accordingly, allowance is believed to be in order and an early notification to that effect would be appreciated.

Please direct all further communications in this application to:

Alisa A. Harbin, Esq.
Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097
Telephone: (510) 923-2708
Facsimile: (510) 655-3542.

Respectfully submitted,

Date: 7/8/02

By: _____

Roberta L. Robins
Registration No. 33,208
Attorney for Applicant

CHIRON CORPORATION
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The second paragraph on page 18 has been amended as follows:

After lysis of the red blood cells, spleen cells from individual rats were cultured in media alone or restimulated *ex vivo* with 2 μg of p227Kb for 6 to 12 hours in culture media (50% RPMI 1640 and 50% alpha-MEM, 10% heat-inactivated fetal bovine serum (FBS), 5 x 10^{-5} M 2β-mercaptoethanol and 1% antibiotics) containing 50 U/ml of rIL-2 (Chiron) and 3 μM monensin (Pharmingen). The p227Kb peptide is an HCV NS5a-specific CTL eptitope with the amino acid sequence AQALPVWAR (SEQ ID NO:3) from the HCV NS5a protein. Splenocytes were stained according to Pharmingen's protocol for surface CD8 with peridinin-chlorophyll protein (PerCP)-conjugated anti-mouse CD8 (Pharmingen), and for intracellular IFN-γ and TNF-a with phycoerythrin (PE)-conjugated anti-mouse IFN-γ and TNF-a (Pharmingen). Peridinin-chlorophyll proteins Cells were analyzed on a FACScalibur. The number of events acquired was such that at least 10,000 CD8+ cells were acquired for each sample. Data files were analyzed using the CellQuest software.

In the Claims:

Claims 1, 3, 14 and 15 have been amended as follows:

1. (Amended) A method for preparing a non-human animal for screening for agents that modulate tolerance to an immunogen comprising the steps of

preparing a nucleic acid directing expression of said immunogen, and

exogenously delivering said nucleic acid to the liver of said animal by portal vein injection, under conditions that result in the sustained expression of the immunogen in the liver thereby inducing immunological tolerance to said immunogen.

3. (Amended) A method for preparing a non-human animal for screening for agents that modulate tolerance to an immunogen comprising delivering said immunogen to the liver of said animal by portal vein injection under conditions that result in sustained presence of said immunogen thereby inducing immunological tolerance to said immunogen, and wherein said delivery is not by expression of a nucleic acid present in the germline of said animal.

14. (Amended) The method of claim [12] 1, wherein said screening is for agents that modulate tolerance to a viral immunogen, and said animal is tolerant to said viral immunogen.

15. (Amended) The method of claim [13] 3, wherein said screening is for agents that modulate tolerance to a viral immunogen, and said animal is tolerant to said viral immunogen.

Claims 8 and 9 have been canceled.